

REMARKSI. Status of the application

Claims 1-17, 22-23, 25-29, 35, 37-40, 42-45 and 47-49 are pending. Claims 18-21, 24, 30-34, 36, 41 and 46 have been cancelled. The Examiner has rejected claims 1-6, 9, 15, 17 and 27-29 and objected to claims 7, 8, 10-14, 16, 22, 23, 25, 26, 35, 37-40, 42-45 and 47-49 as based upon on rejected claims.

II. Rejection under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claim 1 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that in claim 1, the term “=O” is indefinite. While Applicants believe one skilled in the art would understand that this indicates that “Z” in the side chain of the compound of formula (Ia) is -C(O)R₆, Applicants have amended the term “=O” to “oxo” in rejected claim 1 to clarify the claimed subject matter. Applicants have also made similar amendments in claims 2, 3, 6 and 9, all of which also contain this term.

The Examiner has rejected claims 2-5 under 35 U.S.C. § 112, second paragraph, stating that there is insufficient antecedent basis for the limitation “formula __,” recited in the preamble of claims 2-5. Applicants have amended each of these claims into independent format to clarify the claimed subject matter and obviate the antecedent-basis rejections.

The Examiner has rejected claims 6, 9, 17 and 27-29 under 35 U.S.C. § 112, second paragraph, stating that the phrase “fimbrolide derivative” is indefinite because it is not a statutory class of invention. The Examiner suggests the use of the phrase “fimbrolide composition.”

Applicants have amended the rejected claims by replacing the term “fimbrolide derivative” with a reference to the specific compound, thus clarifying the claimed subject matter and more clearly reciting a statutory class of invention.

The Examiner has rejected claims 6 and 9 under 35 U.S.C. § 112, second paragraph, stating that the term “compounds” is indefinite. The Examiner suggests the use of the phrase “a compound.” Per the Examiner’s suggestion, Applicants have amended the term “compounds” to “compound” in the rejected claims.

The Examiner has rejected claim 15 under 35 U.S.C. § 112, second paragraph, stating that the phrase “A method for forming a fimbrolide analogue derived from a compound of formula (III)” is indefinite. The Examiner suggests the phrase “a compound” or a “composition.” Per the Examiner’s suggestion, Applicants have amended claim 15 to replace the rejected terminology with the word “compound.”

Additionally, Applicants have made other amendments to further clarify the claimed invention. None of the amendments made in this response substantively alter the scope of the claimed invention or introduce new matter into the amended claims.

In view of the above amendments and remarks, Applicants respectfully request that the Examiner withdraw the 35 U.S.C. § 112, second paragraph, rejections.

III. Conclusion

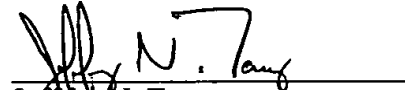
Applicants respectfully request reconsideration of this application in view of the above amendment and remarks.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned, “Version with markings to show changes made.”

Except for issue fees payable under 37 C.F.R. §1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No. 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. §1.136(a)(3).

Respectfully submitted,

MORGAN, LEWIS & BOCKIUS LLP



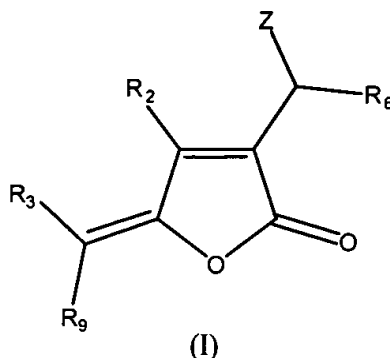
Jeffrey N. Townes
Reg. No. 47,142

Dated: January 3, 2003

Customer No. 009629
MORGAN, LEWIS & BOCKIUS LLP
1111 Pennsylvania Ave., N.W.
Washington, D.C. 20004
202.739.3000

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. A compound according to formula (I):



wherein R_6 is H, OH, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic;

R_2 and R_3 are independently or both H or halogen;

R_9 is halogen;

Z is independently selected from [the group] R_6 , halogen, OOH, $OC(O)R_6$, $[=O]$ oxo, amine, azide, thiol, mercaptoalkyl, alkenyloxy, mercaptoalkenyl, aryloxy, mercaptoaryl, arylalkyloxy, mercaptoarylalkyl,

$SC(O)R_6$, $OS(O)R_6$, $OS(O)_2R_6$, $NHC(O)R_6 = NR_4$ or NHR_4 ; and

R_4 is OH, alkyl, alkoxy, poly(ethylene glycol), alkenyl, aryl or arylalkyl, provided that:

when R_6 is propyl, R_2 is Br, R_3 is H or Br and R_9 is Br, then Z is other than H, $OC(O)CH_3$ or OH;

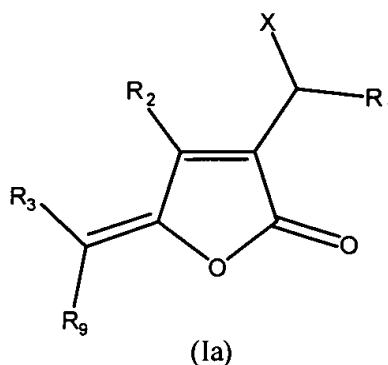
when R_6 is propyl, R_2 is Br, R_3 is H and R is I, then Z is other than $OC(O)CH_3$ or OH;

when R_6 is propyl, R_2 is Br, R_3 is H and R is Cl, then Z is other than OH;

when R_6 is propyl[.], R_2 is H, R_3 and R are Br, then Z is other than H; and

when R_6 is propyl, R_2 is Br, R_9 is Cl and Z is H, then R_3 is other than Cl.

2. A compound according to [claim 1 of] formula (Ia):



wherein R_1 is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic;

X is a halogen, OH, OOH, $OC(O)R_1$ or $[=O]$ oxo;

R_2 and R_3 are independently or both hydrogen or halogen; and

R_9 is halogen,

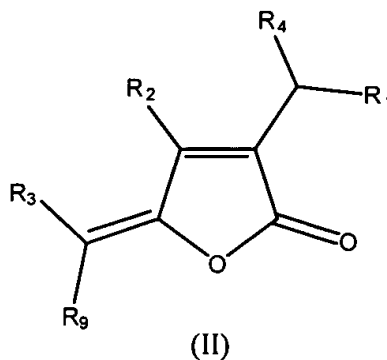
provided that:

when R_1 is propyl, R_2 is Br, R_3 is H or Br and R_9 is Br, then X is other than $OC(O)CH_3$ or OH;

when R_1 is propyl, R_2 is Br, R_3 is H and R_9 is I, then X is other than $OC(O)CH_3$ or OH; and

when R_1 is propyl, R_2 is Br, R_3 is H, R_9 is Cl, then X is other than OH.

3. A compound according to [claim 1 of] formula (II):



wherein R_1 is hydrogen, unsubstituted or substituted, straight chain or branched chain,

hydrophobic, hydrophilic or fluorophilic alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl;

R_2 and R_3 are independently or both hydrogen or halogen;

R_9 is halogen; and

R_4 is selected from halogen, amine, azide, hydroxyl, thiol, or [any] hydrophobic, hydrophilic or fluorophilic alkyl, alkoxy, mercaptoalkylalkenyloxy, mercaptoalkenyl, aryloxy, mercaptoaryl, arylalkyloxy, mercaptoarylalkyl, $OC(O)R_1$, $SC(O)R_1$, $OS(O)R_1$, $OS(O)_2R_1$, $NHC(O)R_1$, $OC(O)NHR_1$, or $[=O]$ oxo,

provided that:

when R_4 is propyl, R_2 is Br, R_3 is H or Br, and R_1 is Br, then R_1 is other than H, $OC(O)CH_3$ or OH;

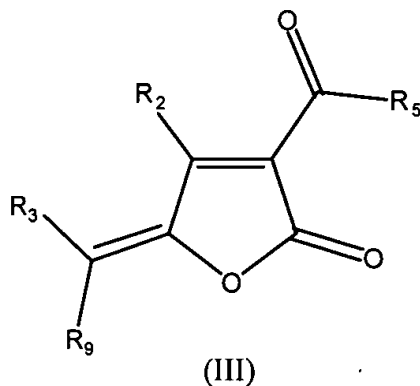
when R_4 is propyl, R_2 is Br, R_3 is H, R_9 is I, then R_1 is other than $OC(O)CH_3$ or OH;

when R_4 is propyl, R_2 is Br, R_3 is H, R_9 is Cl, then R_1 is other than OH;

when R_4 is propyl, R_2 is H, R_3 and R_9 are Br, then R_1 is other than H; and

when R_4 is propyl, R_2 is Br, R_3 and R_9 are Cl, then R_1 is other than H.

4. A compound according to [claim 1 of] formula (III):



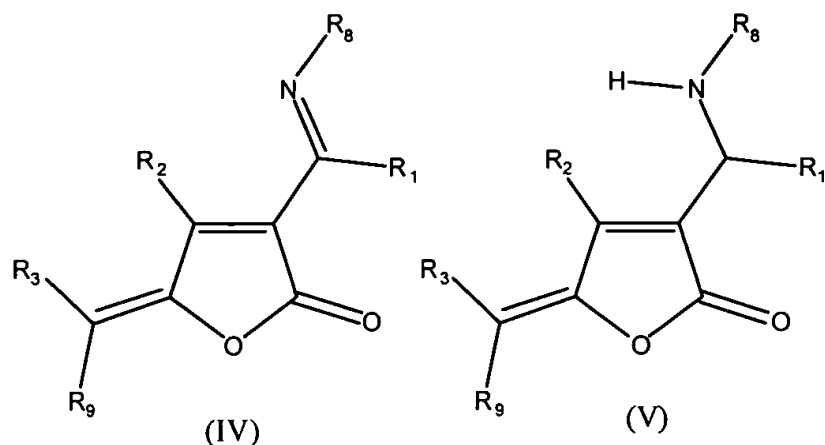
wherein R_2 and R_3 are independently or both hydrogen or halogen;

R_5 is OH or the same as R_1 ;

R_9 is halogen; and

R_1 is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic.

5. A compound according to [claim 1 of] formula (IV) or (V):



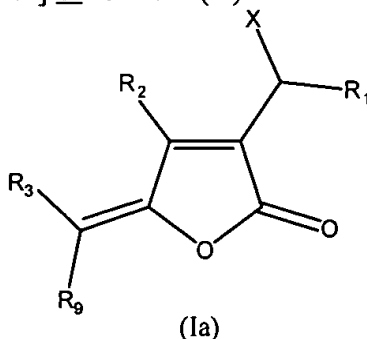
wherein R_1 is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic;

R_2 and R_3 are independently or both hydrogen or halogen;

R_9 is halogen; and

R_8 is OH, NHR_1 , $NHC(X)NH_2$, $NHC(X)NHR_1$ [(X=O, S, NR_1)] or [any] R_1 [.] where X is O, S or NR_1 .

6. A method for forming a [fimbrolide derivative]compound of formula (Ia), the method [including] comprising reacting a fimbrolide with a halogenating agent and/or an oxygenating agent to form the compound[s] [with] of formula (Ia):

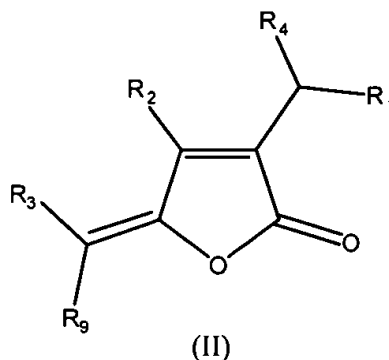


wherein R_1 is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic; X is a halogen [(X = F, Cl, Br or I)], OH, OOH [.] $OC(O)R_1$ or [=O]oxo];

R_2 and R_3 are independently or both hydrogen or halogen; and

R_9 is halogen.

9. A method for forming a [fimbrolide derivative] compound of formula II, the method [including] comprising [displacement] displacing and/or [functionalisation of] functionalizing [the] a halogen or oxygen substituent in the side chain of a fimbrolide compound [side chain] by treating the fimbrolide compound with a nucleophile or an electrophile to form the compound of [compounds with] formula (II):



wherein R₁ is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic;

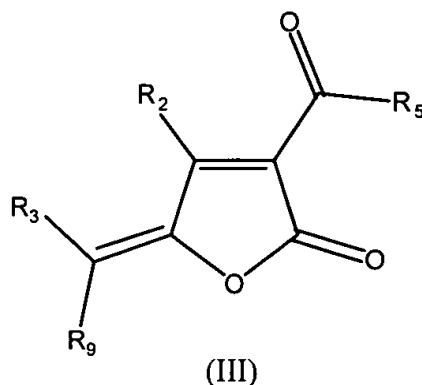
R₂ and R₃ are independently or both hydrogen or halogen;

R₉ is halogen; and

R₄ is selected from [the group] halogen, amine, azide, hydroxyl, thiol, or any hydrophobic, hydrophilic [of] or fluorophilic alkyl, alkoxy, mercaptoalkyl, alkenyloxy, mercaptoalkenyl, aryloxy, mercaptoaryl, arylalkyloxy, mercaptoarylalkyl, OC(O)R₁, SC(O)R₁, OS(O)R₁, OS(O)₂R₁, NHC(O)R₁, OC(O)NHR₁, or [=O] oxo.

provided that when R₄ is propyl, R₂ is Br, R₃ and R₉ are Cl, then R₁ is other than H.

12. A method for forming a [fimbrolide derivative] a compound of formula (III), the method [including] comprising reacting an hydroxyl substituent in the side chain of a fimbrolide [side chain] with an oxidising agent to form [a] the compound in accordance with formula (III):



wherein R_2 and R_3 are independently or both hydrogen or halogen;

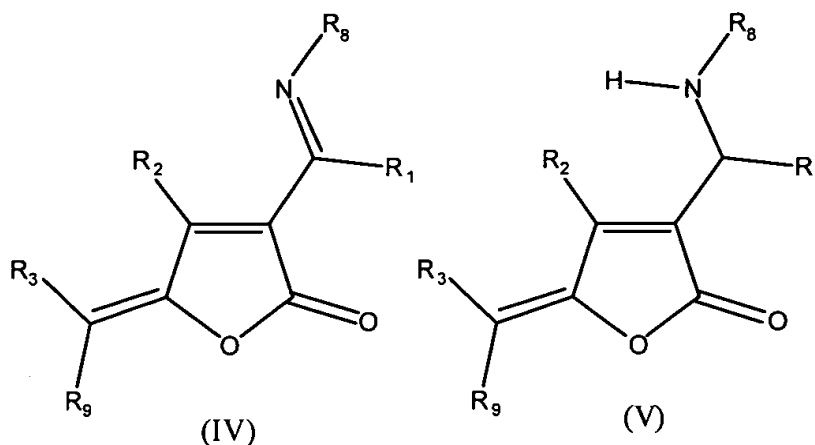
R_5 is OH or the same as R_1 ;

R_9 is halogen; and

R_1 is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic.

14. A method according to claim 13, wherein the acid dichromate agent is selected from the group consisting of a Jones reagent, pyridinium chlorochromate, and pyridinium dichromate.

15. A method for forming a [fimbrolide analogue] compound of formula (IV) or (V), comprising reacting an aldehyde or ketone substituent in the side chain --C(O)R₅ of compound (III) with an amine to [derived] from a compound of formula [(III)] (IV) or (V), wherein formula (IV) and (V) are represented by:



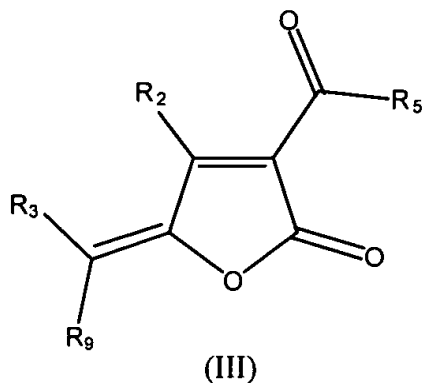
wherein R₁ is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic;

R₂ and R₃ are independently or both hydrogen or halogen;

R₉ is halogen; and

R₈ is OH, NHR₁, NHC(X)NH₂, NHC(X)NHR₁ [(X=O, S, NR₁)] or [any] R₁ where X is O, S or NR₁;

and wherein formula (III) is represented by:



wherein R₂ and R₃ are independently or both hydrogen or halogen;

R_5 is OH or the same as R_1 ;

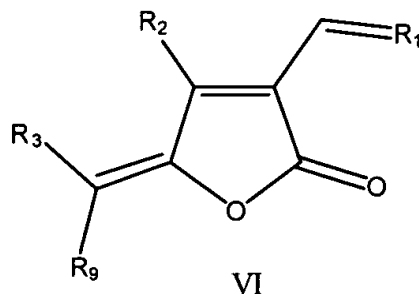
R_9 is halogen; and

R_1 is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic, [the method including reacting an aldehyde or ketone substituent in the fimbrolide side chain – $C(O)R_5$ of the compound (III) with an amine derivative to form a compound with of formula (IV) or (V)]

16. A method according to claim 15, wherein the amine [derivative] is selected from [the group] hydroxyl amine hydrochloride, alkyl and aryl hydrazines, alkyl or aryl amine, optionally in the presence of a reducing agent.

17. A [fimbrolide derivative] compound produced by [a] the method [in accordance with] of claim 6.

25. A compound of formula (VI):



wherein R_1 is alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic;

R_2 and R_3 are independently or both hydrogen or halogen; and

R_9 is halogen.

27. A [fimbrolide derivative] compound produced by [a] the method in accordance with claim 9.

28. A [fimbrolide derivative] compound produced by [a] the method in accordance with claim 12.

29. A [fimbrolide derivative] compound produced by [a] the method in accordance with claim 15.